REMARKS

Applicants would first like to thank Examiner Jeffrey Fredman for granting applicants an interview on July 30, 2004. Claims 1-10, 13, 15, 30-33, 36 and 43-50 were pending in the subject application. Applicants respectfully note that independent claims 1 and 36 have been amended. Support for this amendment may be found, *inter alia*, on page 20, lines 10-14. This amendment does not involve any issue of new matter. Applicant respectfully requests entry of the subject amendment such that claims 1-10, 13, 15, 30-33, 36 and 43-50 will be pending.

2. Applicants acknowledge that the prior rejection over Foulkes in view of Smart has been withdrawn in light of applicant's arguments and claim amendments.

3-4. Obviousness-Type Double Patenting

The Office Action rejects claims 1-10, 13, 15, 30-33, 36, and 43-50 under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-10 of U.S. Patent No. 5,834,188.

In response, without conceding the correctness of this rejection, Applicants will consider submitting a terminal disclaimer, if necessary, to obviate this rejection upon the indication of allowable subject matter.

In addition, applicants respectfully note that since the Office Action does not set forth any grounds of rejection with respect to claims 2-10, 15 and 30-33, aside from the obviousness type double patenting rejection, applicants expect that claims 2-10, 15 and 30-33 will be in condition for allowance if a terminal disclaimer is filed. Applicants further note that if upon entry of this amendment the Examiner mails a second office action setting forth a new ground of rejection for any one of claims 2-10, 15 and 30-33, then the second office action cannot be made final, since applicant's amendment does not necessitate a new ground of rejection *i.e.* any grounds of rejection could have been set forth in the present office action and applicants have not amended claims 2-10, 15 or 30-33.

5-6. 35 U.S.C. 102(e)

The Office Action rejects claims 1, 13, 36, 45-47, 49 and 50 under 35 U.S.C. 102(e) as allegedly anticipated by Harris et al. (U.S. Patent 6,083,690).

In response, applicants submit that the '690 patent does not anticipate the claimed invention. The '690 patent relates to the identification of osteogenic agents using response elements from the promoters of morphogen genes themselves *i.e.* transcription response elements that are present in the DNA sequences of morphogen genes such as those from the mouse BMP-4A gene; it does not describe transcription response elements from downstream genes which are regulated by morphogens *i.e.* genes that are downstream in the signal transduction pathway. Accordingly, there is a distinction between applicant's claimed invention and the teachings of the cited patent: applicant's claims recite methods of identifying agents based on their ability to induce expression of a reporter gene, where the reporter gene is operably-linked to a transcription response element from a gene whose expression is regulated by a morphogen; the '690 patent relates to the identification of agents based on their ability to induce expression of a reporter gene that is operably-linked to a transcription response element of a morphogen gene itself.

Column 4, lines 32-42 of the '690 patent makes this point very clear, reciting as follows:

> The present invention is distinguished from other techniques for identifying bone-active compounds, as it specifically identifies chemical compounds, agents, factors or other substances which stimulate bone cells to produce the bone growth factors in the bone morphogenetic protein (BMP) family (hereinafter "osteogenic agents"). These osteogenic agents are identified by their capacity to increase the activity of the promoters of genes of members of the BMP family and other bone growth factors which are normally produced by bone cells, and other cells including cartilage cells, tumor cells and prostatic cells. (Emphasis added).

The '650 patent further states that on column 2, lines 33-40, as follows:

> Also provided in accordance with the present invention are isolated DNA sequences encoding a promoter region of at least one bone morphogenetic protein, and a system for identifying osteogenic agents comprising an expression vector comprising such promoter sequences operatively linked to a reporter gene encoding an assayable product, and means for detecting the assayable product produced in response to exposure to an osteogenic compound. (Emphasis added).

In contrast, Applicant's claims recite the transcription response elements of the downstream genes which morphogen proteins regulate, not promoter regions or transcription response elements from morphogen genes.

The prior version of applicant's claim 1 recited "a transcription activating element responsive to said morphogen". However, the Examiner appears to be misreading the claim as if it read "a transcription activating element from said morphogen gene", as evident on page 4, lines 3-6 of the office action. In this section, the Examiner listed specific elements of the claimed invention and pointed to passages in the '690 patent allegedly teaching these elements. With regard to the element "a transcription activating element responsive to said morphogen", the examiner points to column 51, claim 1 and column 4, lines 55 to column 5, line 35 of the '690 patent, where the Examiner alleges that "Harris expressly contemplates the use of promoters from genes including BMP-2, BMP-3, BMP-4, BMP-5, BMP-6..." (emphasis added).

Although Applicants consider the prior version of the claims sufficiently clear, they have nevertheless amended claims 1 and 36 in accordance with Examiner Fredman's suggestions during a telephonic interview with the undersigned on July 30, 2004, to recite "a transcription activating element that is responsive to, and distinct from the gene encoding, said morphogen". Since the '690 patent does not teach or suggest a transcription activating element that is responsive to said morphogen, let alone one that is distinct from the gene encoding said morphogen, it cannot

anticipate the claimed invention. Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

7-11. 35 U.S.C. 103(a)

(a) The Office Action rejects claims 1, 13, 36, 45-47, 49 and 50 under 35 U.S.C. 103(a) as allegedly obvious over the '690 reference in view of Smart (U.S. Patent 5,650,276).

In response, applicants respectfully traverse the Examiner's rejection. MPEP 706.02(j) requires, among other things, that the prior art references must teach or suggest all the claim elements in order to establish a *prima facie* case of obviousness. As described in the preceding section, the '690 patent fails to teach or suggest all the claim elements, and in particular fails to teach a screening method using a downstream transcription activating element that is responsive to the morphogen as recited in the claims 1 and 36, from which claims 13, 45-47, 49 and 50 depend. Smart describes methods of screening candidate compounds for the ability to modulate the level of a morphogenic protein, but does not teach or suggest a method of modulating the expression of genes which are themselves regulated by morphogens using a transcription activating element that is responsive to, and distinct from the gene encoding, said morphogen. More importantly, the combination of the '690 patent and Smart fail to teach or suggest this element of the claimed invention and thus does not render the claimed invention obvious. Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

(b) The Office Action rejects claims 1, 13, 36, 43-47, 49 and 50 under 35 U.S.C. 103(a) as allegedly obvious over the '690 patent in view of Smart (U.S. Patent 5,650,276) and further in view of Nadal-Ginard (WO94/18239). As described in the preceding section, the combination of the '690 patent and the Smart fail to teach or suggest all the claim elements, and in particular, fail to teach a screening method using a downstream transcription activating element that is responsive to, and distinct from the gene encoding, the morphogen as recited in claims 1 and 36, from which claims

13, 43-47, 49 and 50 depend. More importantly, the combination of the '690 patent, Smart and Nadal-Ginard fail to teach or suggest this element of the claimed invention and thus does not render the claimed invention obvious. Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

(c) The Office Action rejects claims 1, 13, 36, 45-50 under 35 U.S.C. 103(a) as allegedly obvious over the '690 patent in view of Smart (U.S. Patent 5,650,276) and further in view of Ozkaynak (U.S. Patent 5,652,118). As described in the section (a) above, the combination of the '690 patent and Smart fail to teach or suggest all the claim elements, and in particular, fail to teach a screening method using a downstream transcription activating element that is responsive to, and distinct from the gene encoding, the morphogen as recited in claims 1 and 36, from which claims 13, 45-50 depend. More importantly, the combination of the '690 patent, Smart and Ozkaynak fail to teach or suggest this element of the claimed invention and thus does not render the claimed invention obvious. Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

Applicant believes no fee is due with this response in addition to the three-month extension of time fee. However, if additional fees are due, please charge our Deposit Account No. 18-1945, under Order No. JJJ-P02-540 from which the undersigned is authorized to draw.

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Respectfully submitted,

By _____

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